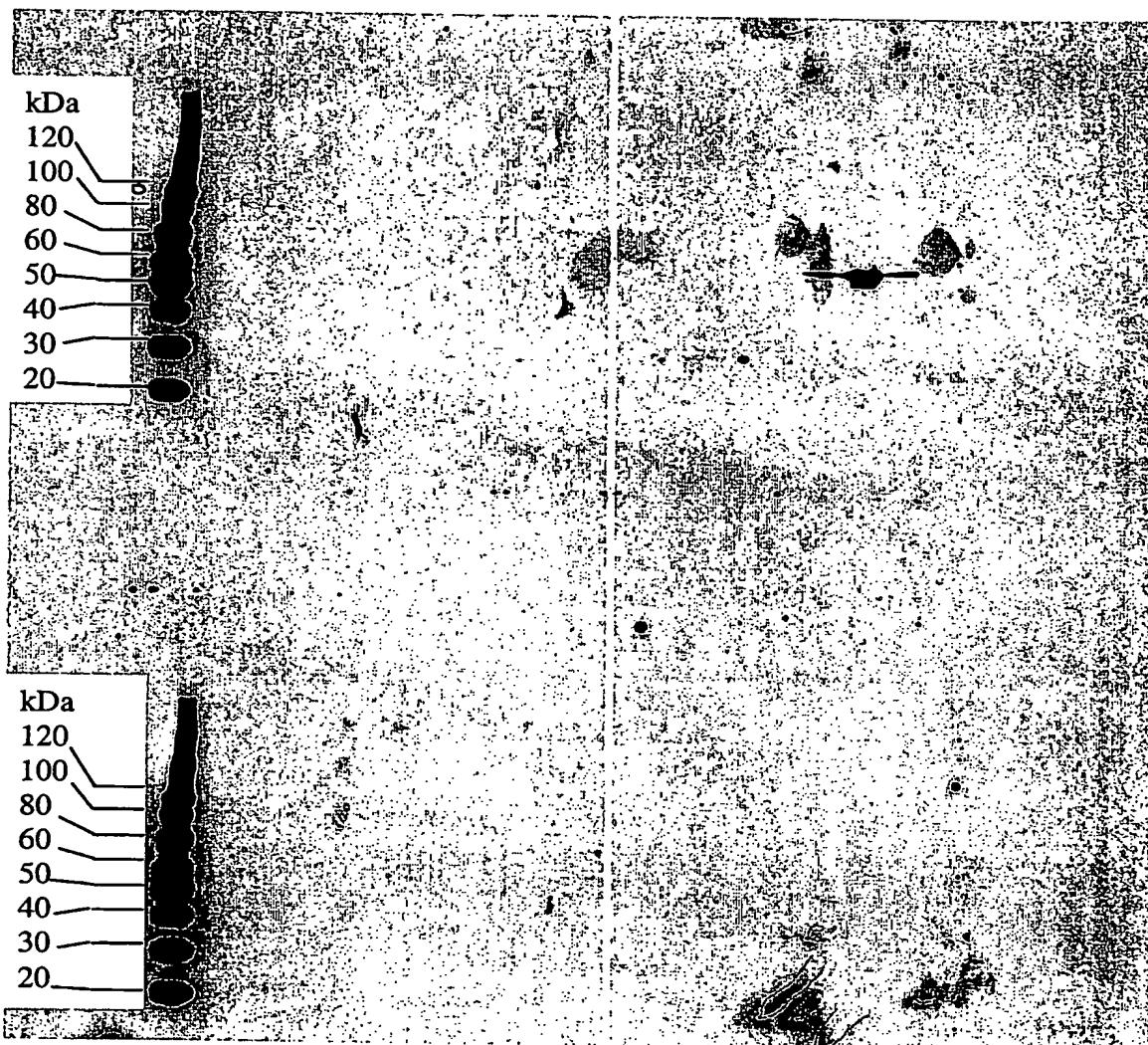
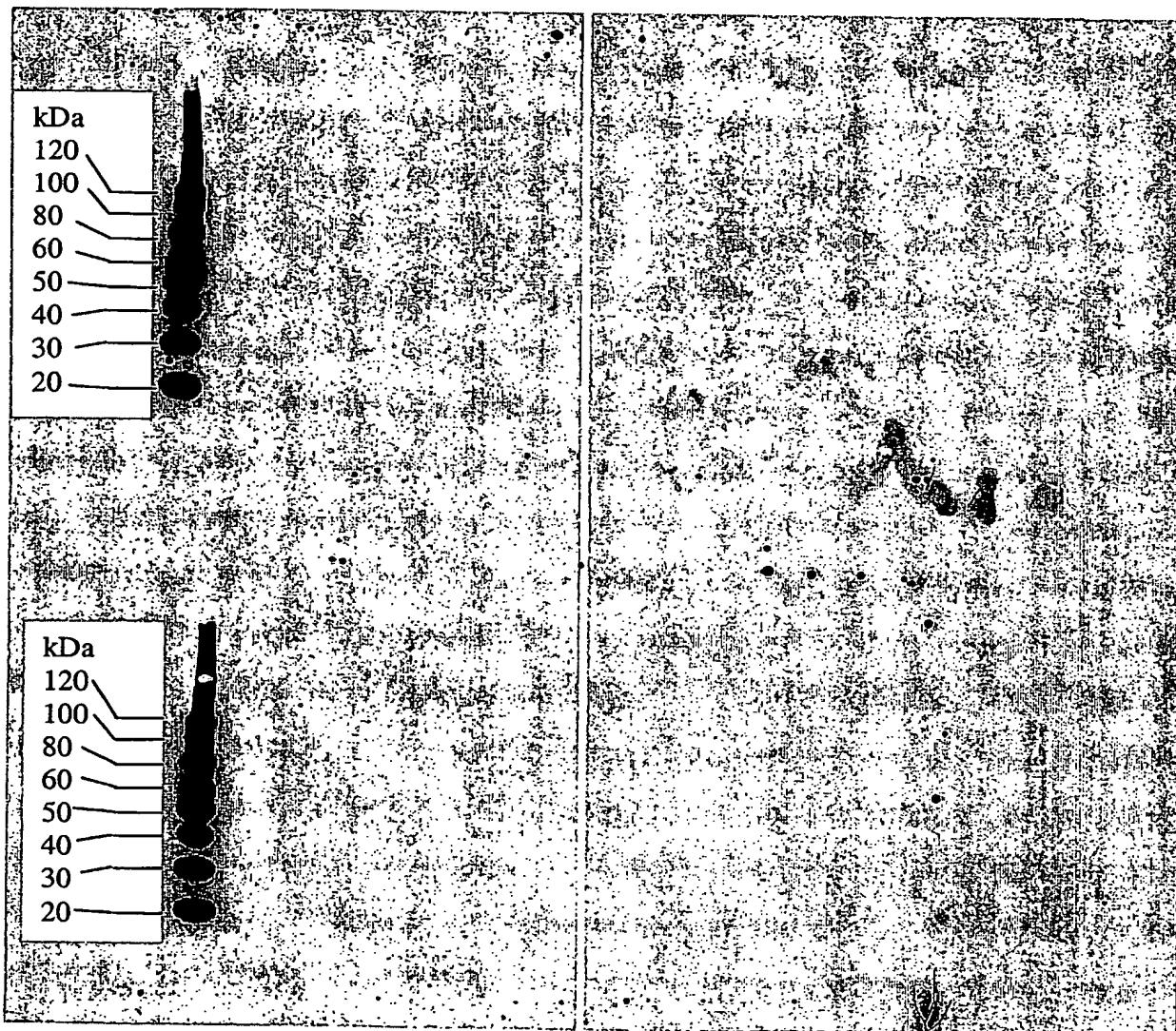


**Figure 1 a****Detection of PDE4D7****Media and intima, balloon-injured, left carotis**

**Figure 1 b****Detection of PDE4D7****Media, non-injured, left carotis****Media, non-injured, right carotis**

**Figure 2****A. 4D5 N-terminus in man and rat**

4D5 N-terminus: 98.85% identical

HUM.seq x RAT.seq                  April 1, 2003 17:04 . . .

```

1 MAQQ.TSPDTLTVPEDNPHECPNPWLNEGLVKSIRENLLQHEKSKTARKS 49
||| ||||||||||||||||| ||||||||||||||||| |||||||||||||||||
1 MAQQTTSPDTLTVPEDNPHECPNPWLNEGLVKSIRENLLQHEKSKTARKS 50

50 VSPKLSPVISPNSPRLLRRMSSNIPKQRRFTVAHT 87
||| ||||||||||||||||| ||||||||||||||||| |||||||||||||
51 VSPKLSPVISPNSPRLLRRMSSNIPKQRRFTVAHT 88

```

**B. Conserved sequence elements in the human PDE4 gene family**

Comparisons:

## UCR1

|   | A | B    | C    | D    |
|---|---|------|------|------|
| A | + | 83.1 | 79.3 | 79.7 |
| B |   | +    | 79.3 | 86.4 |
| C |   |      | +    | 86.2 |
| D |   |      |      | +    |

## UCR2

|   | A | B    | C    | D    |
|---|---|------|------|------|
| A | + | 88.6 | 78.2 | 84.8 |
| B |   | +    | 79.5 | 89.9 |
| C |   |      | +    | 83.3 |
| D |   |      |      | +    |

## Catalytic domain

|   | A | B    | C    | D    |
|---|---|------|------|------|
| A | + | 86.3 | 82.1 | 85.2 |
| B |   | +    | 80.1 | 87.4 |
| C |   |      | +    | 84.6 |
| D |   |      |      | +    |

Figure 3/1

**Q8CG05 - Mouse; Q8CG04 - Rat; Q8IVD2 - Human**

|               |   |
|---------------|---|
| TR_ROD_Q8CG05 | MERDTCDVLS RSKSASEETL HSCNEEEDPF RGMEPYLVRR LSSRSIQLPP        |
| TR_ROD_Q8CG04 | MERNTCDVLS RSKSASEETL HSCNDEEDEPF RGMEPYLVRR LSSRSIQLPP       |
| TR_HUM_Q8IVD2 | MKRNTCDLLS RSKSASEETL HSSNEEEDPF RGMEPYLVRR LSCRNIQLPP        |
|               |   |
| TR_ROD_Q8CG05 | <u>LAFRQLEQAD LRSESENIPR PTSPLPKILP LIAVTSADSS GFDVDNGTSA</u> |
| TR_ROD_Q8CG04 | <u>LAFRQLEQTD LRSESENIPR PTSPLPKILP LIAVTSADST GFDVDNGTSA</u> |
| TR_HUM_Q8IVD2 | <u>LAFRQLEQAD LKSESENIPR PTSPLPKILP LIAITSAESS GFDVDNGTSA</u> |
|               |   |
| TR_ROD_Q8CG05 | GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSMRNSS        |
| TR_ROD_Q8CG04 | GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSMRNSS        |
| TR_HUM_Q8IVD2 | GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSMRNSS        |
|               |   |
| TR_ROD_Q8CG05 | IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP        |
| TR_ROD_Q8CG04 | IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP        |
| TR_HUM_Q8IVD2 | IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP        |
|               |   |
| TR_ROD_Q8CG05 | SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM        |
| TR_ROD_Q8CG04 | SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM        |
| TR_HUM_Q8IVD2 | SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM        |
|               |   |
| TR_ROD_Q8CG05 | LNRELTHLSE MSRSGNQVSE YISNTFLDKQ HEVEIPSPTQ KEKEKKRPM         |
| TR_ROD_Q8CG04 | LNRELTHLSE MSRSGNQVSE YISNTFLDKQ HEVEIPSPTQ KEKEKKRPM         |
| TR_HUM_Q8IVD2 | LNRELTHLSE MSRSGNQVSE FISNTFLDKQ HEVEIPSPTQ KEKEKKRPM         |
|               |   |
| TR_ROD_Q8CG05 | SQISGVKKLM HSSSLTNSCI PRFGVKTEQE DVLAKELEDV NKWGLHVFRI        |
| TR_ROD_Q8CG04 | SQISGVKKLM HSSSLTNSCI PRFGVKTEQE DVLAKELEDV NKWGLHVFRI        |
| TR_HUM_Q8IVD2 | SQISGVKKLM HSSSLTNSSI PRFGVKTEQE DVLAKELEDV NKWGLHVFRI        |
|               |   |
| TR_ROD_Q8CG05 | AELSGNRPLT VIMHTIFQER DLLKTFKIPV DTLITYLMTL EDHYHADVAY        |
| TR_ROD_Q8CG04 | AELSGNRPLT VIMHTIFQER DLLKTFKIPV DTLITYLMTL EDHYHADVAY        |
| TR_HUM_Q8IVD2 | AELSGNRPLT VIMHTIFQER DLLKTFKIPV DTLITYLMTL EDHYHADVAY        |
|               |   |
| TR_ROD_Q8CG05 | HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN        |
| TR_ROD_Q8CG04 | HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN        |
| TR_HUM_Q8IVD2 | HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN        |

Figure 3/2

|               |  |
|---------------|--|
| TR_ROD_Q8CG05 | QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS |
| TR_ROD_Q8CG04 | QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS |
| TR_HUM_Q8IVD2 | QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS |
|               |  |
| TR_ROD_Q8CG05 | LRKMVIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV |
| TR_ROD_Q8CG04 | LRKMAIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV |
| TR_HUM_Q8IVD2 | LRKMVIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV |
|               |  |
| TR_ROD_Q8CG05 | LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD |
| TR_ROD_Q8CG04 | LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD |
| TR_HUM_Q8IVD2 | LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD |
|               |  |
| TR_ROD_Q8CG05 | KHNASVEKSQ VGFIDYIVHP LWETWADLVH PDAQDILDTL EDNREWYQST |
| TR_ROD_Q8CG04 | KHNASVEKSQ VGFIDYIVHP LWETWADLVH PDAQDILDTL EDNREWYQST |
| TR_HUM_Q8IVD2 | KHNASVEKSQ VGFIDYIVHP LWETWADLVH PDAQDILDTL EDNREWYQST |
|               |  |
| TR_ROD_Q8CG05 | IPQSPSPAPD DQEEGRQQQT EKFQFELTLE EDGESDTEKD SGSQVEEDTS |
| TR_ROD_Q8CG04 | IPQSPSPAPD DQEDGRQQQT EKFQFELTLE EDGESDTEKD SGSQVEEDTS |
| TR_HUM_Q8IVD2 | IPQSPSPAPD DPEEGRQQQT EKFQFELTLE EDGESDTEKD SGSQVEEDTS |
|               |  |
| TR_ROD_Q8CG05 | CSDSKTLCTQ DSESTEIPLD EQVEEEAVAE EE.SQPETCV PDDCCPDT   |
| TR_ROD_Q8CG04 | CSDSKTLCTQ DSESTEIPLD EQVEEEAVAE EE.SQPQTGV ADDCCPDT   |
| TR_HUM_Q8IVD2 | CSDSKTLCTQ DSESTEIPLD EQVEEEAVGE EEESQPEACV IDDRSPDT   |

**Figure 4:**

anti-PDE4D5

1 2 3 4 5 6 7 8 9 10 11 12

120  
100  
80  
60  
50  
40  
30  
20120  
100  
80  
60  
50  
40  
30  
20

1 2 3 4 5 6 7 8 9 10 11 12

anti-PDE4D7

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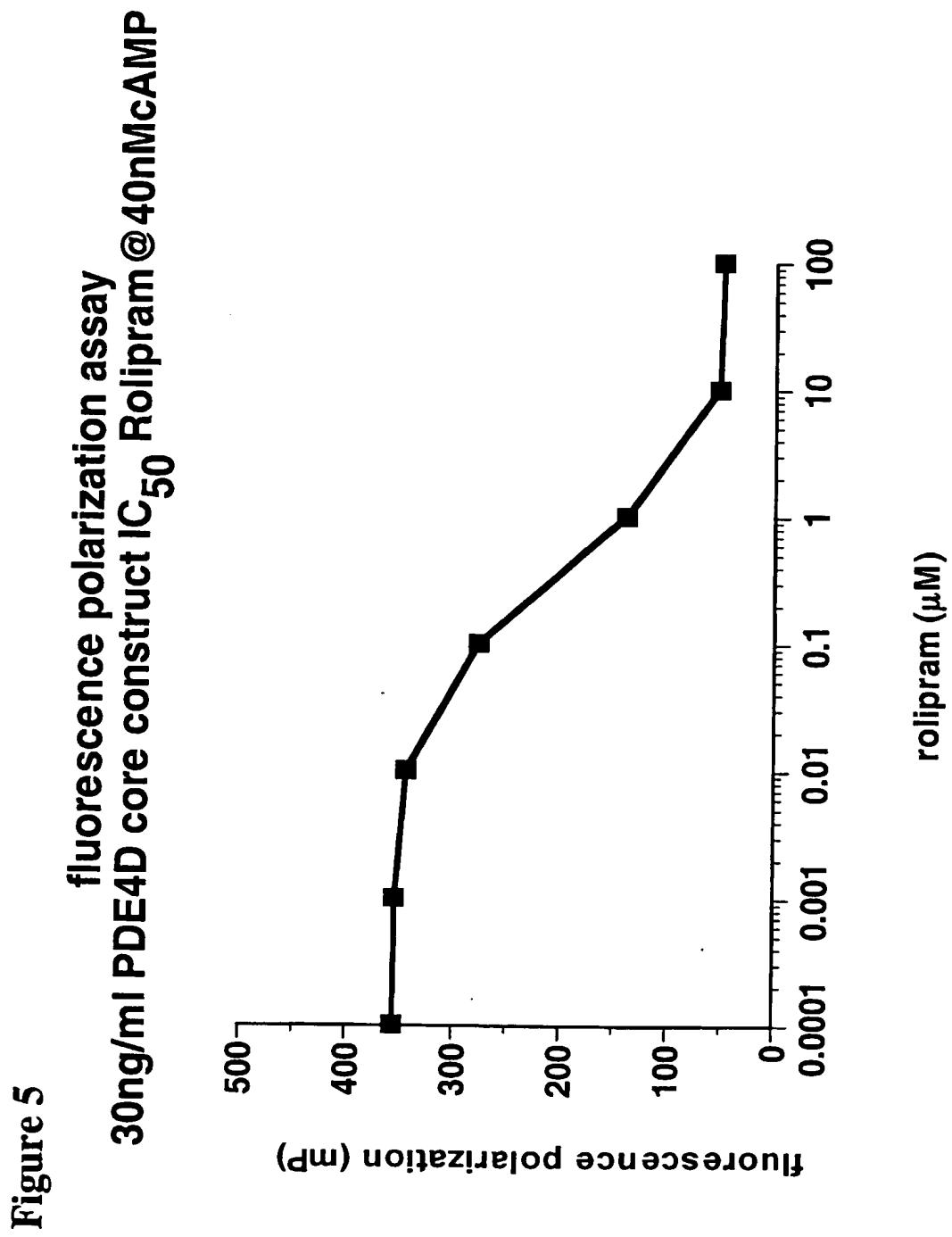


Figure 6

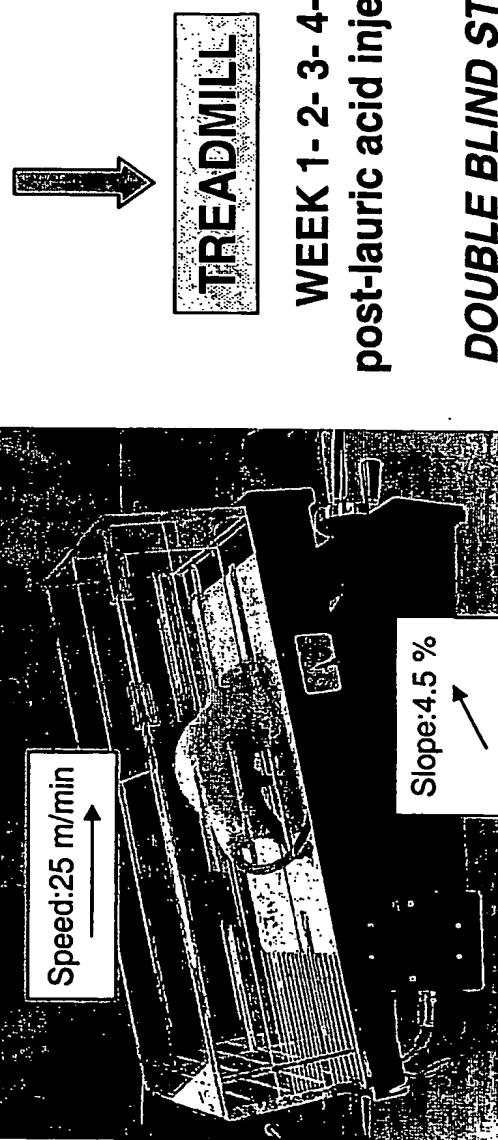
**L/R FEMORAL ARTERY  
INJECTION**

---

| TREATMENT (p.o)       |                                    |
|-----------------------|------------------------------------|
| <b>Group 1 (n=12)</b> | <b>Sham operated</b>               |
| <b>Group 3 (n=12)</b> | <b>Lauric Acid (75 µg)</b>         |
| <b>Group 3 (n=12)</b> | <b>Lauric Acid (75 µg)</b>         |
| <b>Group 4 (n=12)</b> | <b>Lauric Acid (75 µg)</b>         |
|                       | <b>Placebo (vehicle)</b>           |
|                       | <b>Placebo (vehicle)</b>           |
|                       | <b>Cilomillast (8 mg/kg/day)*</b>  |
|                       | <b>Cilostazol (100 mg/kg/day)*</b> |

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\*first dose administered 24 h and 2 h pre-LA injection



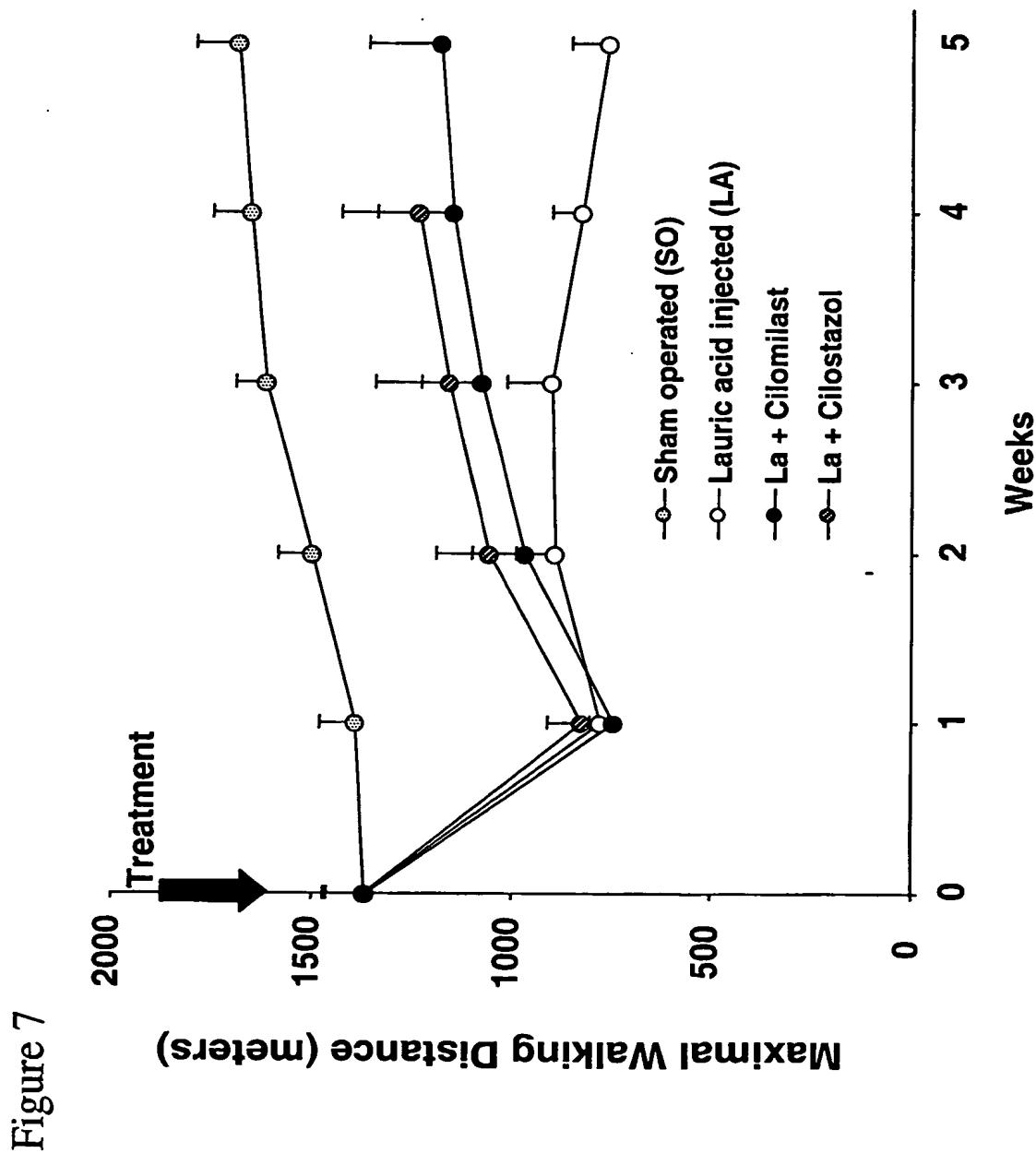
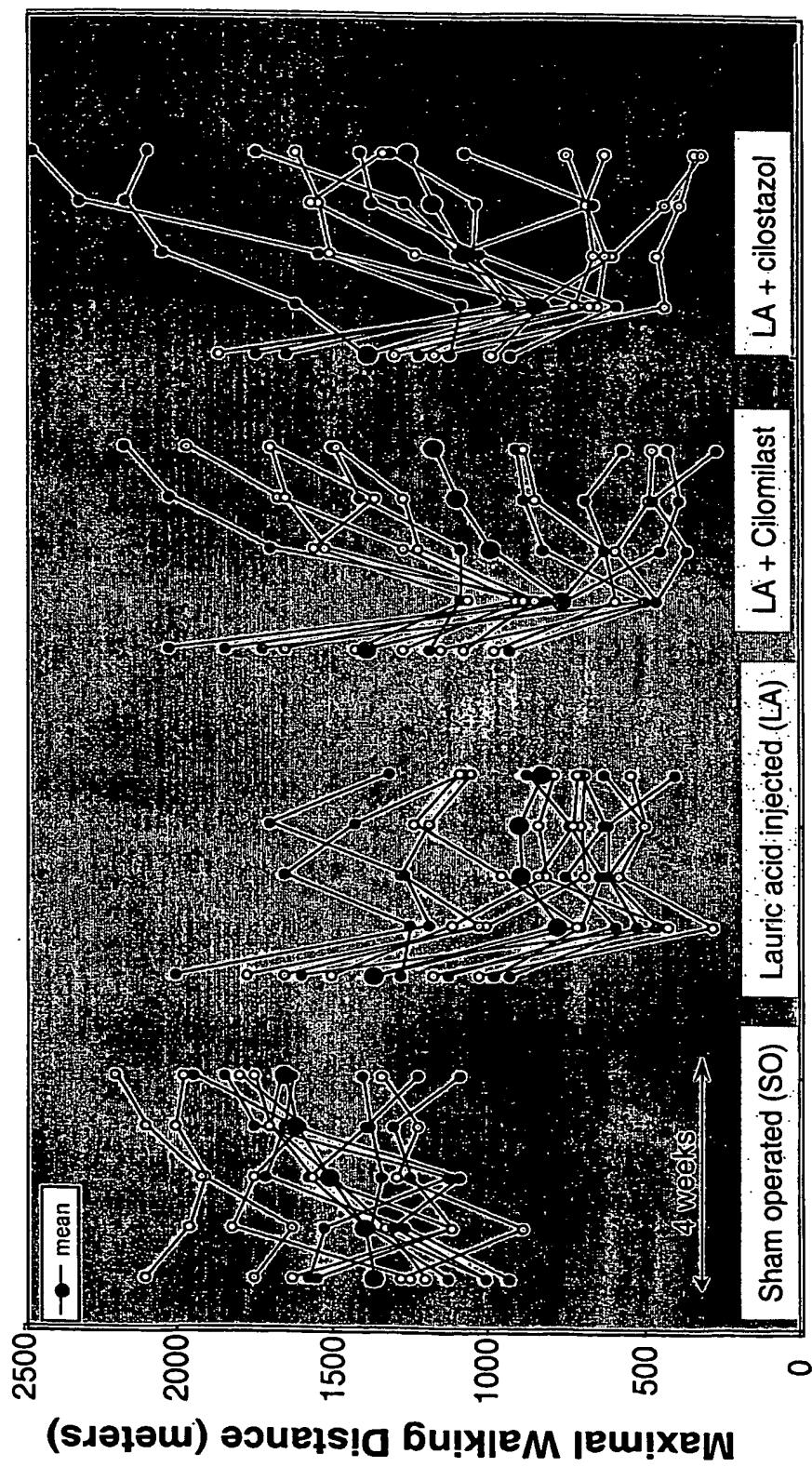


Figure 8

## Individual Results\*



\*N = 12 rats per group

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Figure 9

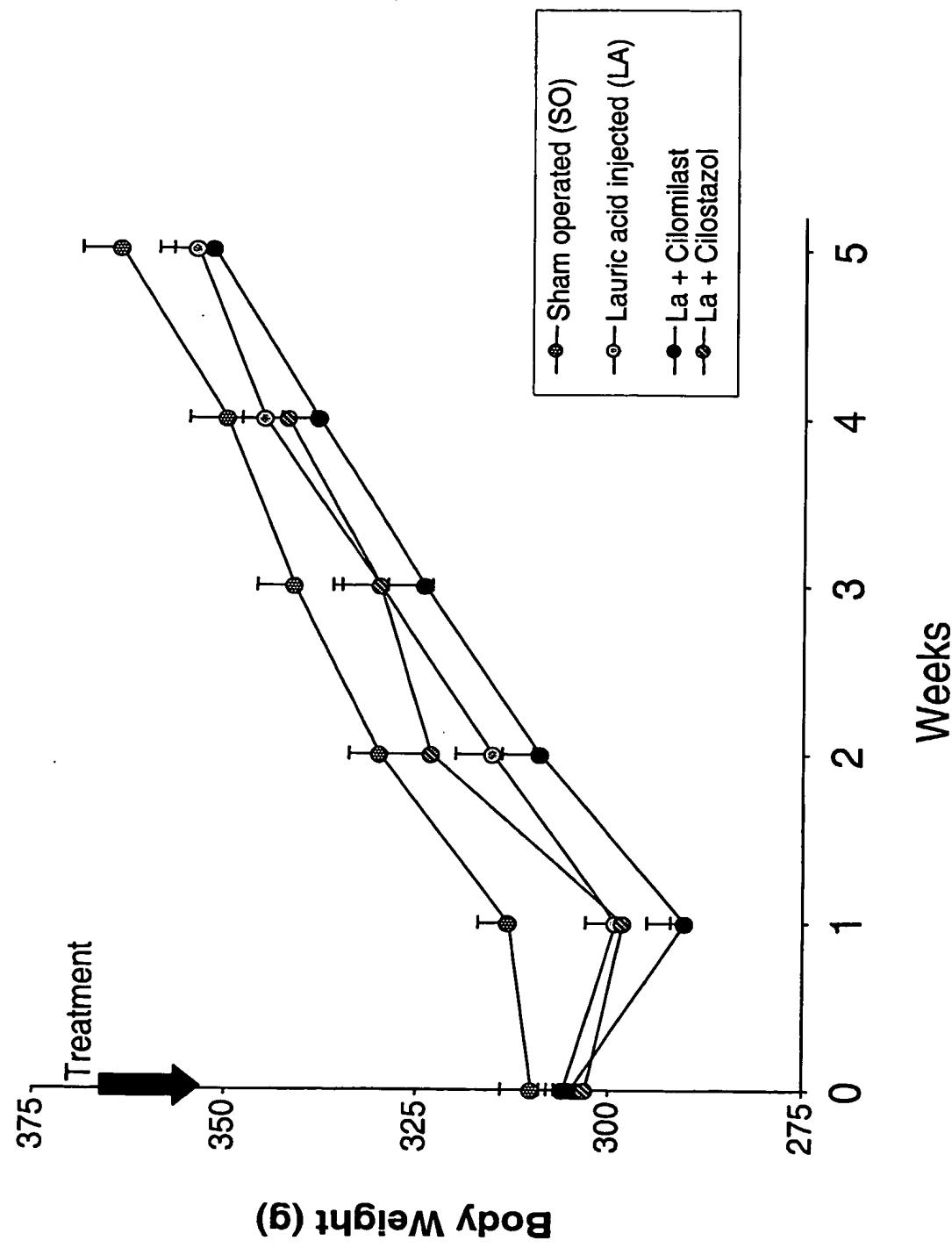


Figure 10

Figure 11

